AIDS: CAN WE BE POSITIVE?

By Neville Hodgkinson

The Sunday Times (London) 26 April 1992

It hardly sounds possible. After worldwide campaigns for "safer sex", and eight years of anti-viral research and treatment costing billions of pounds, a growing number of senior scientists are challenging the idea that the human immunodeficiency virus (HIV) causes AIDS.

The idea seems outrageous to doctors who have seen their patients fall sick and die after becoming infected with the virus, which was discovered in 1983.

Scientists believed HIV was a new, sexually-transmitted disease, and predicted that it would eventually put the sexually-active population at risk. But the failure of the epidemic to "explode" into the general population has encouraged some experts to ask whether a simple cause-and-effect link between HIV and AIDS really exists.

They do not question the existence of the disease called AIDS the acquired immune deficiency syndrome in which the body's normal deaga a variety of infections, and some rare cancers, cease to work. What they are saying is that new ideas are emerging that question the extent of HIV's role in AIDS.

Some of these scientists now suggest that the virus can be harmless on its own, but may play a part in throwing the immune system into disarray when other infections are present. This could mean some people who are HIV-positive will never fall ill.

That in itself is dramatically different frm the view held for years by most AIDS scientists: that the presence of HIV in the body is a time-bomb which sooner or later will explode, seeking out and destroying all the body's T-cells, an essential part of the immune system.

But other sceptics go further. They argue that the virus is not new, that it is not normally sexually transmitted, and that it is almost certainly harmless almost no different from scores of other innocuous viruses in the same class that may have been around for centuries, but which have only come to light recently because of modern techniques of analysis.

They do not deny that HIV is usually present in people whose immune systems have failed, but argue that this is because those people have been exposed to special health risks that bring them into contact with many infectious agents.

To explain the AIDS epidemic, many favour an idea originally proposed when the first cases were discovered in a group of male homosexual drug users with devastating bacterial and other infections: that a dangerous lifestyle, rather than a new microbe, is mostly to blame.

Some believe the main factor is the unprecedented level of drug use, both inhaled and injected, during the 1970s and 1980s and more recently, inappropriate use of medical drugs in trying to

counter AIDS.

Other victims, such as haemophiliacs, transfusion recipients and babies born to drug-abusing or otherwise sick mothers, have suffered illnesses that in the past would have been attributed to their physical condition or circumstances, the sceptics argue. Being exposed to other people's blood means their chances of showing antibodies to a wide variety of infectious agents, including HIV, are much higher than average. So are their chances of falling ill but not for reasons that need have anything to do with HIV.

Six million Africans have been shown to be HIV-positive, according to the World Health Organisation. But again, a long-awaited explosion of AIDS has not happened, the dissident scientists claim. In all, 120,000 AIDS cases have been reported during the past eight years. That is a small percentage of the total number of deaths that could be expected anyway over that period out of a 6m-strong group.

African "AIDS" victims suffer from a completely different pattern of illnesses to those in the West: largely old African diseases such as slim disease, fever, diarrhoea and tuberculosis, usually associated with malnutrition, parasitic infections and poor sanitary conditions. They are being rediagnosed as AIDS because virus-hunters can point to the presence of HIV, the critics argue.

According to this view, the entire edifice of international alarm and expenditure surrounding HIV is based on a faulty premise: that HIV is a new, deadly virus. If the critics prove to be right, the HIV-AIDS link would be seen as the biggest medical and scietific blunder this century.

While many AIDS scientists now accept that HIV cannot work as simply as originally believed, they regard those who say it has nothing to do with AIDS as irresponsible "flat-earthers" who do not deserve to be taken seriously.

The leading dissident, Dr Peter Duesberg, professor of molecular biology at the University of California in Berkeley, has lost his $350,000 "outstanding investigator" funding from the National Institutes of Health, the American government's premier scientific research organisation. In a letter cancelling his grant, officials referred to his recent research as being "less productive, perhaps reflecting a dilution of his efforts with non-scientific issues".

Some of the dissidents say they have had their work boycotted, and become marginalised from mainstream scientific meetings.

To try to break through this impasse, nearly 50 biomedical scientists, statisticians and other professionals have come together to form an international body, The Group for the Scientific Reappraisal of the HIV/AIDS-Hypothesis. Some are to take part in an "alternative" AIDS symposium in the Netherlands next month.

They are also launching a newsletter, Rethinking AIDS, that will examine the scientific basis for claims made about AIDS and propose experiments for testing the HIV theory.

It is edited by a molecular biologist, Dr Harvey Bialy, scientific editor of the journal BioTechnology, a sister publication to Nature.

Asked why such a publication was needed, Bialy said: "The vast majority of instruments of public information, as well as the majority of scientists involved in biomedical research, have indiscriminately subscribed to a single hypothesis, that a virus called HIV is the cause of the

disease syndrome called AIDS.

"The hypothesis has become all things to all people. It violates everything we previously knew about virus disease, and allows any kind of therapy, any kind of research, to generate research bucks.

"What kind of science continues to place all its marbles, all its faith, all its research bucks, in such a theory?

"The answer I keep coming back to is that it has nothing to do with science; the reasons are all unscientific.

"We have taken sex and equated it with death, and into that mixture we have thrown money. What an ugly stew."

The new group has been trying to persuade a leading medical or scientific journal to publish a letter outlining its concerns. It states:

"It is widely believed by the general public that a retrovirus called HIV causes the group of diseases called AIDS. Many biomedical scientists now question this hypothesis. We propose that a thorough reappraisal of the existing evidence for and against this hypothesis be conducted by a suitable independent group. We further propose that critical epidemiological studies be devised and undertaken."

None of the journals approached so far has been willing to publish this letter, despite several distinguished signatories.

"It's frozen out," says Dr Charles Thomas, the group's co-ordinator, a former professor of biological chemistry at Harvard University who now heads the Helicon Foundation, a non-profit research organisation.

Yet he says he is unable to name "a single scientific publication that purports, either convincingly or unconvincingly, to demonstrate that HIV causes AIDS it's really a quite extraordinary story".

Another leading scientist in the group, Dr Kary Mullis, inventor of the polymerase chain reaction (PCR) technique, a breakthrough in genetic testing now used worldwide, also questions the HIV hypothesis, but says other experts are unwilling to because so many livelihoods and reputations depend on it.

"I can't find a single virologist who will give me references which show that HIV is the probable cause of AIDS," he says.

"On an issue as important as this, there should be a set of scientific documents somewhere, research papers written by people who are accessible, demonstrating this. But they are not available. If you ask a virologist for that information, you don't get an answer, you get fury."

Few voices have dared question the HIV hypothesis. Notable exceptions include Gordon Stewart, emeritus professor of public health at Glasgow University, who says he has been repeatedly frustrated in his attempts to publicise inconsistencies and inadequacies in the conventional view; and writer Jad Adams, whose 1989 book AIDS: The HIV Myth described how an "AIDS Establishment" had come into being, committed to the HIV hypothesis and

fiercely resisting anyone who challenged it.

Meditel, a small medical documentary film-making company, has produced three films challenging the AIDS orthodoxy, shown on Channel 4's Dispatches programme. The second of these, The AIDS Catch, shown in June 1990, was bitterly attacked by leading figures from the Medical Research Council, and was reported to the Broadcasting Complaints Commission by the Wellcome Foundation, manufacturer of the anti-AIDS drug AZT, and the Terrence Higgins Trust, the AIDS group. The commission partially upheld the complaints, but its findings were rejected by the Independent Television Commission and Channel 4 itself.

The belief that HIV is the cause of AIDS has become so axiomatic for most doctors working in the field that they view any suggestion to the contrary as dangerously irresponsible.

Yet several observations support the view that HIV can no longer be considered a lone, infectious assassin. Originally, it was thought that the virus killed billions of T-cells, vital to the body's immune defences. Later studies have shown it is active in only one in 10,000 T-cells, far fewer than would be needed to kill off the cells faster than the body replaces them.

About 97% of all American AIDS patients are from abnormal health risk groups: heterosexual intravenous drug users, male homosexuals who use oral aphrodisiacs and psychoactive drugs, haemophiliacs, babies of drug-addicted mothers and recipients of blood transfusions. And about 91% of American AIDS patients are males. If the disease is sexually transmitted, why do so few women (other than drug users, and some from ethnic minority groups in poverty-stricken circumstances) develop AIDS? It cannot be because of the spread of "safer sex" conventional venereal diseases and unwanted pregnancies are increasing.

With every year that goes by, the length of time the virus is said to take before it produces disease has had to be extended. Even assuming that HIV causes AIDS, on the basis of present statistics it will take 33 years for most HIV-positive haemophiliacs in America to develop the disease. That compares with original predictions of three to five years.

Fewer than 50% of American AIDS patients are tested for HIV the diagnosis is made on the basis of their disease symptoms. And of those who are tested, 5% never show signs of HIV infection. It means that even if HIV does cause AIDS, there are other causes as well.

Many other agents shown to cause suppression of the body's immune defences are present in AIDS patients. These include immunological response to semen following anal intercourse; use of recreational rugs such as nitrites ("poppers"); chronic antibiotic use (often associated with promiscuity); opiate drugs; repeated blood transfusions; anaesthetics; malnutrition (whether caused by bowel dysfunction in homosexuals, drug use, poverty or anorexia nervosa); multiple infections by diverse micobes; and infection by specific viruses such as cytomegalovirus, Epstein-Barr virus, and hepatitis B virus.

When chimpanzees are infected experimentally with HIV they do not develop AIDS. Even a monkey equivalent of HIV, called simian immunodeficiency virus (SIV), does not cause disease when carried by monkeys living in the wild.

Healthy HIV-positive mothers can give birth to healthy babies, and some HIV-positive babies have so far never developed AIDS-related symptoms.

Out of several thousand reported cases of needle injuries and cuts among health workers and laboratory researchers handling HIV-contaminated material, only 5% have become HIV-

positive; and of those, only one person lacking other identified risks has developed AIDS.

AIDS-type diseases were reported for at least 100 years before 1980.

None of this proves that HIV cannot cause AIDS, says another of the critics, Dr Robert Root-Bernstein, associate professor of physiology at Michigan State University and a prize-winning researcher in immunology. But he argues in a paper entitled Do We Know The Cause(s) of AIDS? published in the specialist journal, Perspectives in Biology and Medicine, that "premature closure of inquiry lays us open to the risk of making a colossal blunder".

On April 23, 1984, Margaret Heckler had an announcement as dramatic and rewarding as any politician could wish to make. The American secretary for health and human services told a press conference in Washington, DC, that Dr Robert Gallo, a senior researcher at the National Cancer Institute, had found the virus responsible for AIDS.

It was the news all America, but especially the homosexual community, with 2,000 dead from AIDS and 100 new cases being reported every week, had been anxiously awaiting.

It was also desperately important to the Western medical and scientific community, whose proud record of mastery over microbial enemies was being challenged by AIDS.

Heckler reflected these powerful emotions accurately. "Today we add another miracle to the long honour roll of American medicine and science," she said. "Today's discovery represents the triumph of science over a dreaded disease.

"Those who have disparaged this scientific search those who have said we weren't doing enough have not understood how sound, solid, significant medical research proceeds."

A blood test for the virus would be available within months, she said, and a vaccine ready for testing within two years.

The blood test did indeed arrive, and became the basis of a multi-million-dollar industry. Gallo had already developed it, and a patent was filed the same day as Heckler's announcement.

As he strode into the press conference, Gallo was a picture of confidence, fastidiously dressed. "He approached the podium like the only kid in the school assembly to have won a national merit scholarship," a journalist, David Black, wrote later.

"His manner seemed to me condescending, as though he were the Keeper of Secrets obliged to deal with a world of lesser mortals."

The scientific world seemed hypnotised by his certainty, and Gallo's conviction that HIV alone explained the arrival of AIDS "who needs co-factors when you've been hit by a truck?" he is quoted as saying became the established view.

Eight years on, Gallo's superstar status and scientific credibility have been undermined. The scientific community has now accepted that the virus was first isolated in 1983 by a group led by Dr Luc Montagnier at the Institut Pasteur in Paris, and had been sent to Gallo's laboratory for further testing.

A National Institutes of Health inquiry panel has accused Gallo of "intellectual appropriation" of the virus. It says that an article announcing the discovery published in Science magazine in

1984, of which Gallo was joint author, contained "misrepresentations or falsifications" of methodology and data.

Gallo, who also faces federal inquiries alleging perjury and fraud in his patent application, denies any intention to mislead and blames the errors in the article on the rush to publish.

For American telvision viewers, however, his decline from fame was encapsulated earlier this month as he was chased by a camera crew with the interviewer demanding: "Did you steal the virus, Dr Gallo? Did you steal the virus?"

Perhaps as significant as Gallo's fall from grace is a sharp shift in Montagnier's position on AIDS. As one of the speakers at the "alternative" symposium next month, he will be outlining his current view that HIV can be a benign, "peaceful" virus, which only becomes dangerous in the presence of other organisms (see story on below).

"We were naive," he says."We thought this one virus was doing all the destruction. Now we have to understand the other factors in this."

Montagnier first made some of his views on these "co-factors" known at the sixth international AIDS conference in San Francisco nearly two years ago, seven years after his original discovery of HIV. He thought his message would be a bombshell. But it was not one the conference wanted to hear.

Of 12,000 delegates present, only 200 went to hear his talk. By the time he had finished, almost half of those had walked out. His views were dismissed by leading American AIDS scientists and public health officials.

"There was Montagnier, the Jesus of HIV, and they threw him out of the temple," one observer commented.

Peter Duesberg was puzzled by Heckler and Gallo's 1984 announcement. As the first scientist to map the genetic structure common to all retroviruses, of which HIV is one, he knew that mice and chickens, for example, contain 50 to 100 retroviruses that never cause disease.

He knew that if you look hard enough, "when you're in the retrovirus business you can detect a retrovirus". But attempts to prove that the viruses cause disease have uniformly failed, according to Duesberg. He wondered what was so special about this new one that could make it the cause of AIDS. Three years later, he challenged the HIV-AIDS hypothesis on biological grounds in the specialist journal, Cancer Research.

The response from other medical scientists was dismissive. While it was not known how HIV could be so devastating, they argued that the epidemiological evidence studies of what was actually happening in people showed such a close link between HIV and AIDS that the virus was clearly to blame.

Now Duesberg has returned to the attack with an 8,000-word critique in the Paris-based journal, Biomedicine and Pharmacotherapy. In it he maintains that not only the virology, but also the patterns of illness in the American and European AIDS epidemics, fail to support the theory that HIV is responsible.

He says that in he seven years since HIV testing became available, the official estimate of the number of Americans carrying the virus has stayed constant, at about 1m. Screening by the US

Army among potential recruits has also shown a constant proportion of both men and women 0.03% with antibodies to HIV.

Neither of those observations is consistent with the arrival of a new, infectious disease, Duesberg says, for which cases would be expected to spread exponentially in susceptible populations.

The explanation that best fits the data, Duesberg now says, is that HIV is not new "it is perhaps as old as America". He thinks it survives naturally, at a low level, by being passed from mothers to their children, as is the case with most retroviruses.

The fact that the 0.03% figure is equal in men and women indicates that it is reflecting this harmless "background" HIV. It is unrelated to AIDS, for which the vast majority of American victims are men.

The HIV-positive babies seen by health authorities are different: they come mainly from drug-abusing parents, and it is adverse emotional and physical circumstances, not HIV, that may prove lethal to them. When they come from good homes, or are adopted and well cared for, most stay healthy.

In fact, almost all Americans who develop AIDS have been exposed to abnormal health risks, Duesberg says. The virus acts as a risk "marker". The medical profession's mistake has been to jump to the conclusion that when that marker is present, the patient's illness is a consequence of it.

One way of establishing HIV's role in causing illness would be to compare the progress of carefully matched groups of haemophiliac men, some with HIV and some without. No such study has been published.

There is, however, a group of 32 haemophiliacs in Edinburgh who are all thought to have been exposed to a single contaminated batch of Factor VIII, the blood-clotting substance in which their own bodies are deficient, in 1984. Eighteen became HIV-positive, and 10 of those have developed immune deficiencies. The other 14 did not, and all of those have stayed well.

That seemed to demonstrate that HIV must be responsible. But last November, doctors reported in The Lancet that as a group, the 10 differed from the others in that their immune systems were hyperactive before they became infected with HIV.

The doctors suggested this might be a genetic trait predisposing to HIV disease. For Duesberg, it supports other evidence that haemophiliacs develop immune deficiencies not because of HIV, but because of their condition and its treatment. Their regular transfusions cause repeated challenges to their immune system. Other studies have shown that the length of time they have been receiving these transfusions is their biggest risk factor for developing immune disorders.

If the real cause of haemophiliac AIDS is haemophilia, how come their wives occasionally die of AIDS after sexual transmission of HIV?

The answer, according to Duesberg, is that they don't. The US Centres for Disease Control has reported that a total of 94 wives of haemophiliacs have been diagnosed with "AIDS" diseases in the past seven years, on average about 13 a year. Although HIV is difficult to transmit sexually, requiring on average about 1,000 sexual contacts, some of the wives have become HIV-positive.

But about 80 deaths a year could be expected anyway in this group, on the basis of standard death rates. And the wives don't get illnesses such as Kaposi's sarcoma, or dementia, or lymphoma, or wasting syndrome, which currently account for 39% of all American AIDS diseases.

"What you see here are pneumonias, mostly, and a few other infections typical diseases of older age. Normal morbidity and mortality may be the simplest explanation, but because they are the wives of haemophiliacs it is called AIDS."

If Duesberg is proved right in believing HIV does not cause AIDS, where does the epidemic come from? In his latest paper, Duesberg claims its origin rests with the explosion in the use of "recreational" drugs; and that in addition it is now being driven by the toxic side-effects of AZT, originally developed as chemotherapy for cancer patients but now prescribed to about 120,000 HIV-positive Americans, and 180,000 people worldwide.

The ability of drugs to break down the immune system is well documented, Duesberg says. "It's not one bath house party, or two, or even 10 or 20, but if you do it over and over and over again. One gay activist in New York says that when he was wild in the bath houses, he had 3,000 sexual contacts.

"You can't do that on testosterone (naturally occurring male hormone).

With testosterone you fall asleep after one or two contacts. But if they are flying on amphetamines and poppers they go in for two or three days, and with 20 or 30 contacts. Poppers sound so cute, but they contain a very reactive compound, which is mutagenic and carcinogenic.

"So they mutate and oxidise and damage their DNA and RNA, and they don't get any sleep, and in the long run if they go on harder drugs such as cocaine and so on they can't pay for their food any more and don't eat the vitamins and proteins they need to regenerate, and they come down in hospital with pneumonia.

"Then along comes Dr Gallo and he looks for a latent retrovirus. Then they give them AZT, which is inevitably toxic, and a year later you are definitely dead."

Duesberg cites several studies in which patients have recovered from AIDS-type illnesses after coming off AZT, which he maintains is "AIDS by prescription".

Tragically, he believes the same could have been true for Kimberley Bergalis, the 23-year-old American student who died four years after having two wisdom teeth extracted by her dentist.

A year after the operation, and shortly before graduating from the University of Florida, Kimberley who was a virgin, and had never injected drugs developed oral thrush. Her health declined further, and doctors considered stress and hepatitis as possible causes. In December 1989 she was found to be HIV-positive, and it was assumed she had picked up the virus from her dentist, a bswhod of AIDS in September 1990.

In a bitter farewell letter, Kimberley wrote of her hair falling out, of losing more than 40lb, of blisters on her sides, of nausea and vomiting, night sweats, chronic fevers, cramping, diarrhoea, acne infesting her face and neck, and of the white fungus, with which her illness had started, running wild.

The world was devastated on hearing what it took to be the horror of AIDS. Yet every one of

these symptoms could readily be attributable to the AZT Kimberley was given to the end because of its known mode of action, Duesberg says. By contrast, no mechanism whereby HIV could produce such symptoms has ever been demonstrated.

The drug theory leaves many questions unanswered. There seems to have been many homosexual victims, for example, who either never took drugs or who gave them up on learning of their antibody status, but who still went into rapid decline.

Duesberg and the other scientists seeking a new look at AIDS admit that their own ideas on its causes are speculative. But they say there should at least be more studies into the specific risks of drugs and other lifestyle factors.

With taxpayer-funded spending on HIV research and the hunt for a vaccine now running at $4 billion a year in America £ 150m a year in Britain, perhaps a wider look at AIDS is overdue.*

TIME TO THINK AGAIN ON AIDS LINK, CLAIMS HIV PIONEER

Life is looking up for Professor Luc Montagnier. After eight years and numerous inquiries, the world scientific community has finally accepted that he was the first scientist to discover the human immunodeficiency virus (HIV), and not Dr Robert Gallo of the US National Institutes of Health.

While Gallo now faces a federal inquiry into allegations of perjury and patent fraud, Montagnier has moved into a new Aids research wing at the Institut Pasteur in Paris, where he is director of cancer research. The institute is suing the American government for millions of dollars in lost royalties arising from the test for detecting the virus.

However, another battle, which Montagnier considers much more important, has yet to be resolved: that of determining exactly how HIV can bring about the conditions in the body that lead to Aids.

Unlike some American critics of the "HIV equals Aids" theory, Montagnier accepts there is "a very strong case that HIV has something to do with Aids; without HIV, I don't think we would have Aids epidemics. There are obvious cases of transmission of Aids from one person to another where HIV was the only risk factor."

But he says some people develop the symptoms of Aids the immune system failing, and infections taking the body over as a result without HIV being present or playing any part in their illness.

Even when the virus is in the body, it may remain "benign", becoming dangerous only in the presence of other organisms.

"HIV infection doesn't necessarily lead to Aids," he said. "There are some people who could escape that. It may be a minority, but we can hope by treatments to increase this number."

Montagnier's theory is that HIV works by triggering changes in the body that may subsequently lead to Aids when other "co-factors" are present. At that point, HIV would not necessarily still be involved. This has important consequences. If he is right, it means a cure is unlikely to be found in the anti-viral programmes, which are the focus of most contemporary Aids research.

But other factors involved in the disease process may offer vital leads for treatment and prevention.

Montagnier insists that contrary to what was originally thought, HIV does not attack cells of the immune system directly.

Instead, he believes that when the virus infects the body in the presence of other microbes, it appears to spark a process in which some of the cells contributing to immune defences against microbial invaders become wrongly "programmed".

Faced with further attack, the immune cells fail to recognise the invaders as foreign. Rather than countering them, they regard themselves as redundant and "commit suicide".

The ability to self-destruct, called apoptosis, is natural to many cells. It forms part of a system of checks and balances that enables the body to maintain itself in good repair.

But in people with Aids, the process has gone haywire. Immune cells are destroying themselves faster than they can be replaced, so eventually the patient is left helpless against a variety of germs that in healthy people do not cause any harm.

Laboratory tests have shown that about 10-20% of the immune cells in HIV-positive people demonstrate a readiness to react in this abnormal way when challenged by other microbes, compared with almost none in healthy people.

That still does not prove HIV is to blame; people infected with HIV may have been infected wlot other "foreign" agents as well. But it puts it under strong suspicion of playing a part.

Now Montagnier is planning a series of trials to test a variety of strategies for redcing the abnormal reaction.

"From our new ideas we can derive some advice, if not some strong proposals, for treating HIV-infected individuals to prevent evolution towards the Aids stage," he said.

"If activation by micro-organisms is important, I think they should reduce their risks of being exposed to such microbes, and have long-term antibiotic treatment."

Other strategies are likely to include dietary advice and vitamin supplements, aimed at easing chemical stresses in the body, which have also been seen to provoke apoptosis.

In good health, the body has its own methods for controlling the process and several new drug treatments, which may make good a deficienc in these controls, are also being explored.

Another possibility is that individual HIV-positive people are vulnerable to specific microbes, depending on what they were harbouring when they first became exposed to HIV. By identifying those in the laboratory, doctors would be able, Montagnier believes, to give very precise prophylactic treatment to prevent the destruction of immune cells.

This new way of looking at Aids also implies there should be great caution over the therapeutic use of any conventionally designed anti-HIV vaccine, Montagnier says, as the vaccine might trigger the very process it should be preventing. "It would be a very small danger for people who haven't seen HIV before, the correct way of using a vaccine, but for people who are HIV-infected I don't think it would be very good to inject them again with the virus protein. That

could make them worse." *

VIRUSMYTH HOMEPAGE